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The JOURNAL *of the Oklahoma State Medical Association*

Volume 48 **JANUARY 1955** Number 1

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Editorials

Orthoëpy and I

It is surprising that the great majority of physicians, traditionally trained to exercise unusual care in the practice of medicine, permit themselves to be careless with medical words. Carelessness in speech is an old American custom. Numerous writers such as Petroleum V. Nasby and George Ade capitalized on this almost universal failing. Currently we are amused by the weird and whimsical pronunciations of our friend Pogo and his Neighbors in Okeefenochee swamp.

It is possible that the common mis-pronunciation of medical words which are used with regularity is because interns and resident staff pronounce words as they hear them used by their senior staff members and perhaps even by their teachers while in medical school. If this be true we should assume an individual responsibility in exercising care in our technical speech. If this were done for one year all of us would profit by having become more proficient in the use of the spoken word.

Just for fun look at the following list of 12 words, pronounce them immediately, and check how you said them on the appropriately phonetically spelled example. Now turn to page 2 where the correct pronunciations are given. If you get eight correct you are very good; ten is excellent and if you get more than ten you may consider yourself to be first-class orthoëpist.

1. Salicylate—(a) sa LIS i late (b) sal i SIL ate (c) SAL i sil ate.
2. Abdomen—(a) AB do men (b) ab DO men (c) ab DOM en.
3. Hyperpnea—(a) hy perp NEE a (b) hy PERP ne a (c) HY perp ne a.
4. Poliomyelitis—(a) Pahl e o my e li tis (b)POLE e o my e li tis (c) pole e o MY e LI tis.
5. Trichomonas—(a) tri KOM o nas (b) tri ko MO nas (c) TRIK o mo nas.
6. Vertebral (a) ver TEE bral (b) VER te bral (c) ver TIB ral.
7. Esophageal—(a) e SOF a je al (b) e sof a JEE al (c) e so FAJ e al.
8. Cavernous—(a) KAV er nus (b) ka VER nus (c) ka VER NUS.
9. Caffein—(a) CAF fe in (b) caf FEEN (c) CAF een.
10. Respiratory—(a) RES pi ra to ry (b) re SPI ra to ry (c) res pi ra TORY.
11. Flaccid—(a) FLAS sid (b) FLAK sid (c) FLAY sid.
12. Menarche—(a) men ARCH (b) men ARK (c) me NAR kah.

If you don't believe it, check the list in a good medical and a good standard dictionary, which reminds us—that is what we started to editorialize about in the first place.

Acute Respiratory Infections

Haight, T. H., Kahn, F. H., and Ziegra, Sumner[1] studied the efficacy of erythromycin and penicillin on ordinary respiratory infections in a group of 269 male navy recruits. The men, as the diagnosis was made, were placed in rotation on erythromycin, penicillin or a placebo. There was no appreciable difference in the course of the illness in any of the three groups except in patients in whom there was a Group A Hemolytic Streptococcal infection. They point out that similar results have been obtained from like studies using aureomycin hydrochloride and oxytetracycline (terramycin).

The difficulty of an accurate clinical diagnosis of a causative organism was apparent in the study. Suggestive evidence of a streptococcal infection aside from laboratory data is an exudative pharyngitis with tender regional lymph nodes. Influenzal infections were accompanied by an increased prevalence of non-productive cough and substernal aching. Most all the patients felt ill; the great majority complained of sore throat, and about two-thirds had either coryza or nasal congestion. Since neither influenzal nor other nonbacterial infections were influenced by the antibiotics used, the differentiation between the two is unimportant. One would, however, like to be able to separate the Group A Hemolytic Streptococcal infections from the non-bacterial. One dif-

1. Armed Forces Medical Journal 5:1405 (Oct.) 1954.

ferential point illustrated by them but not stressed is the effect of both erythromycin and penicillin in streptococcol infections on fever. There was an abrupt drop to near normal within 24 to 48 hours. This would indicate that one is not dealing with a sensitive organism if the temperature persists longer and the value of continued antibiotic therapy is questionable even if apparently indicated at the onset.

From this study the authors conclude: "it appears that the routine use of erythromycin or penicillin in the treatment of viral or related non-bacterial respiratory infections is of little or no value in affecting the acute infection, and for economic and medical reasons should be avoided." They perhaps should have added "in the age group studied."

Another Name But Still Paternalism

The commercial insurance companies and Blue Cross have their collective finger in the dyke against the flood of public demand for social medicine. Such security against the paralyzing cost of serious or protracted illness is desirable. There are facets of this arrangement, however, that smack of a paternalism which, if from statism, we would abhor, and that preclude complete honesty of both the patient and the doctor.

The fact that the patient has hospital insurance and not the nature or seriousness of his sickness may be the determining factor in whether or not he is to be hospitalized. The existence of surgical benefits may similarly affect his decision to be or not to be operated on. Not too long ago the termination of the illness and the ability of the patient to take care of himself at home marked the end of his hospital stay.

The most serious defects in this whole arrangement, which is for the most part quite satisfactory, are the exclusions and the specified stipulated coverages. The doctor, if it is at all possible, will make a diagnosis that will permit the patient to collect on his insurance. There is no quarrel with this, but it does preclude strict medical honesty in the matter of records and perhaps also in thinking.

These insidious inroads on the integrity of our people and our patients would be obviated if the patient had to share somewhat in the financial responsibility, over and above the cost of his premium. If each day in the hospital cost the patient a little bit, he would not go to the hospital unless he needed to nor would he stay longer than necessary. He would, however, be protected against the financial calamity that illness may result in. The insurance carriers might save enough in this manner to eliminate exclusions from their contracts. The will to get well would no longer be lessened by the paternalism of the insurance companies and the doctor could write on the chart what he found and what he thought and not just words acceptable under the patient's contract.

Answers to Diction Quiz

1-c; 2-b; 3-a; 4-a; 5-a; 6-b; 7-c; 8-a; 9-a; 10-b; 11-b; 12-c.

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Scientific Article

ANGIOCARDIOGRAPHY *in Congenital Malformations of the* HEART *and* GREAT VESSELS *Amenable to* SURGICAL CORRECTION

SIMON DOLIN, M.D.

THE AUTHOR

Simon Dolin, M.D., is assistant professor in radiology at the University of Oklahoma School of Medicine. From the Department of Radiology, University and Crippled Children's Hospitals, University of Oklahoma, School of Medicine. Part of this paper was exhibited at the Oklahoma State Medical Association meeting, May, 1954, Oklahoma City, Oklahoma.

Angiocardiography consists of the X-ray examination of the cardiac chambers and great vessels during the opacification by an intravenously injected radio-opaque contrast medium. Serial roentgenograms are obtained at an interval of one half second.

Angiocardiography has been a helpful method in the analysis of the various types of congenital malformations of the heart and in the study of acquired heart diseases as well. During the last decade, it has become a standard clinical procedure and an essential part of the investigative methods of cardio-vascular diseases.

Angiocardiography has contributed toward a more effective interpretation of the conventional fluoroscopic and radiographic examinations of the heart, leading to a better understanding of the physiopathology of the cardiovascular system. Our classical concepts have varied considerably since angiocardiography became an accepted clinical procedure.

The technique of angiocardiography has been simplified by the use of a serial casette changer, allowing multiple fast exposures. With the Fairchild camera one can take two exposures in a second. The contrast medium (Urokon-Sodium 70 per cent) is injected rapidly into the antecubital vein. General anesthesia is preferable for small children, local anesthesia for adults and bigger children. The amount to be injected varies: 40-50 cc. for adults, and 1 cc. per kg. body weight for children. The injection has to be done rapidly, usually within a period of 1.5 to two seconds. As soon as the contrast medium is injected, the exposures are taken in rapid succession, as mentioned above. In an average case, 15 exposures are taken in order to visualize the right and left cardiac chambers, and the great vessels. A roentgenogram of the urinary system may be taken immediately after the angiocardiographic procedure in order to detect any possible abnormalities of the urinary tract.

Sensitivity tests are performed prior to the procedure. The sensitivity test consists of an injection of 0.1 cc. of the contrast medium intradermally or, diluted with saline, intravenously. The patient is observed for 10 to 15 minutes, and in case sensitivity reactions (urticaria, rapid pulse changes, etc.) are noted, the examination is postponed.

Reactions: The usual immediate reaction is the perception of a metallic or bitter taste in the mouth. This is followed by a sensation of intense heat over the entire body. This sensation vanishes after five to 10 minutes. A generalized weakness and a fall in the systolic blood pressure is also noted. Dizziness and vomiting is a rare manifestation.

The greatest value of angiocardiography has been in the diagnosis of congenital malformations of the heart, and especially in the detection and selection of those malformations that are amenable to surgical correction. Recent advances in cardiac surgery have enabled the correction of the following congenital malformations of the heart and great vessels:

Fig. 1 A

Fig. 1 B

Fig. 1 C

1. Pulmonary Artery Stenosis.
   a. Isolated Valvular stenosis
   b. Infundibular stenosis
2. Tetralogy of Fallot.
3. Interatrial Septal Defects.
4. Patent Ductus Arteriosus.
5. Coarctation of the Aorta.
6. Other Congenital Vascular Anomalies.

Isolated Pulmonary Valvular Stenosis

Congenital stenosis of the pulmonary artery is usually associated with other congenital abnormalities such as interatrial septal defects or an overriding aorta. However, recent studies have demonstrated that "isolated" pulmonary stenosis, particularly of the valvular type, is not an uncommon condition. It may be the result of a foetal endocarditis involving the pulmonary cusps after the septa have closed (Abbott), or a developmental arrest (Gross). Above the stenosis the pulmonary artery is generally dilated, giving rise to the so-called "post-stenotic dilation," the exact mechanism of which is not yet entirely clear. The right ventricle and conus are hypertrophic and often dilated.

Cyanosis may never appear or may be slight and late in onset. It depends on the degree of the pulmonary obstruction and it is primarily due to a diminished blood supply to the lungs and the resulting changes of the pulmonary arterioles, and an interference with oxygenation. Clubbing of the fingers is proportional to the cyanosis.

The main symptom is dyspnea on exertion. Epistaxis is not uncommon. A harsh systolic murmur and a systolic thrill are usually perceived in the second left interspace close to the sternum, radiating to the left clavicle and into the left side of the neck. The murmur is often heard over the entire precordium.

Roentgenograms of the chest reveal either a normal or a slightly enlarged cardiac silhouette. Hypertrophy involves the right ventricle, and the apex of the heart may be blunt and turned up. The pulmonary artery segment is prominent. The vascular lung markings are scant, particularly at the periphery. However, good vascularity of the lungs on the roentenogram is by no means contradictory to the diagnosis of pulmonary stenosis, particularly in older children. Collateral circulation via bronchial arteries and also via the collaterals arising from mediastinal, esophageal, internal mammary, pericardial, and other arteries, is early established (Christeller, Ruysch). Electrocardiogram usually shows a right axis deviation.

Cardiac catherization shows normal blood oxygen saturation levels in the chambers of the right heart and pulmonary artery, whereas the pressure in the pulmonary artery is lower than in the right ventricle. The fall in the arterial pressure may be abrupt, indicating the site of the stenosis.

Angiocardiography may demonstrate the actual site of the narrowing, the post-stenotic dilatation of the pulmonary artery, and the right ventricular dilatation.

Surgery is directed toward the correction of the stenosis and the amelioration of the pulmonary circulation. The Brock-Knife valvulotomy is the procedure of choice. The operative results are quite promising and discussion of the latter is beyond the scope of this paper.

Case Report. Case I: A.F. #187-991.

A 14-year old white male exhibited easy fatigability and an exertional dyspnea since the age of five. He had repeated episodes of upper respiratory infections.

A grade III systolic murmur was heard over the entire precordium with the maximum intensity over the second and third intercostal spaces on the left. Blood pressure: 120/80; pulse: 76. EKG: Incomplete right bundle branch block and right ventricular hypertrophy.

Roentgenogram of the chest (Fig. 1, A) revealed an enlargement of the cardiac silhouette. There was a prominence of the pulmonary artery segment and a scarce vascularity of the peripheral parts of the lungs. Angiocardiogram in the left anterior oblique position (Fig. 1, B and 1, C) revealed a stenosis of the pulmonary artery at the valve with a post-stenotic dilation as well as a dilatation of the right ventricle.

Cardiac catheterization revealed a markedly increased pressure in the right ventricle.

The patient was operated and a Brock-Knife valvulotomy for the stenosis of the pulmonary valve was performed. The patient had an uneventful post-operative course and when re-examined a year later, showed considerable symptomatic improvement.

Fig. 2 A Fig. 2 B Fig. 2 C

Infundibular Stenosis of the Pulmonary Artery

Infundibular stenosis of infravalvular stenosis of the pulmonary artery is usually associated with other congenital malformations of the heart, such as interventricular septal defects and overriding aorta, thus forming one of the main components of the tetralogy of Fallot. The degree of stenosis of the conus varies, and in rare cases, the infundibulum may be atrophied, and the conus reduced to a short narrow passage. The pulmonary artery may be dilated distal to the stenosis, the dilatation extending as far as the bifurcation or beyond. In many cases the pulmonary artery is either normal in caliber or hypoplastic throughout its initial course.

The clinical picture in the rare cases of isolated infundibular stenosis resembles the one seen in cases of isolated valvular stenosis, (see above) and depends greatly on the degree of the pulmonary obstruction. The physical findings are essentially the same. Electrocardiogram may show right axis deviation.

Roentgenogram of the chest may show a normal cardiac silhouette or an enlargement of the right ventricle. A concavity at the site of the pulmonary artery segment is usually present resembling the configuration seen in tetralogy of Fallot. The pulmonary vascularity depends on the degree of the collateral circulation.

Cardiac catheterization reveals a gradual fall in the arterial pressure of the pulmonary conus in contrast to a high pressure in the right ventricle.

Angiocardiography may demonstrate the actual narrowing of the infundibulum as well as the right ventricular hypertrophy and, in many cases, establish the presence or confirm the absence of associated anomalies. This is best done with the patient in the RAO position (Marder and Scott) while the valvular stenosis is best demonstrated in the LAO position.

The surgical approach for infundibular stenosis is quite different from the one advocated for valvular stenosis. Hence, the accurate demonstration of the narrowed segment is of paramount importance. Angio-

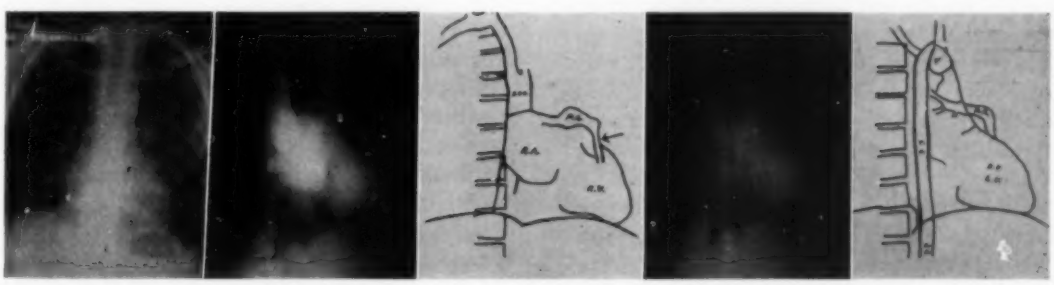

Fig. 3 A Fig. 3 B Fig. 3 C Fig. 3 D Fig. 3 E

cardiography, in association with cardiac catheterization has proven to be an important adjunct towards achieving this purpose. Brock has advocated a new technique for the correction of the infundibular stenosis, consisting of a dilatation of the narrowed segment by a direct approach. The majority of the cardiac surgeons still concur to the Blalock-Taussig operation or to the Potts-Smith operation, and we shall discuss it briefly in the following chapter.

Case Report. Case II: J.W. #190-648.

A four-year old white male had spells of cyanosis since birth and repeated upper respiratory infections. A grade III to IV systolic murmur was heard over the entire precordium with the maximum intensity over the second right intercostal space. EKG: suggestive of right ventricular hypertrophy. Roentgenogram of the chest (Fig. 2, A) revealed a cardiac silhouette within normal limits. There was a concavity at the site of the pulmonary artery segment and diminished vascularity of the lung periphery. Angiocardiogram (Fig. 2, B and 2, C) was performed in the right anterior oblique position and a narrow infundibulum of the pulmonary conus was demonstrated with an enlargement of the right ventricle. Cardiac catheterization revealed hypertension of the right ventricle and possible high inter-ventricular septal defect. The patient was operated and a Blalock-Taussig anastomosis between the left subclavian artery and the pulmonary artery was established in order to relieve the infundibular stenosis. The patient was seen eight months later. with marked clinical improvement.

Tetralogy of Fallot

Tetralogy of Fallot is a congenital heart disease of the cyanotic type. It consists of: 1. Stenosis of the pulmonary artery, 2. Interventricular septal defect, 3. Dextroposition of the aorta (overriding), and, 4. Hypertrophy of the right ventricle. A wide range of variation exists. The variables depend on the degree and on the type of pulmonary stenosis, on the situation of the interventricular septal defect, and on the alterations in the course of the aorta. Most often, the pulmonary conus of the right ventricle is small and hypo-plastic, the infundibulum is narrow, and the initial segment of the pulmonary artery is also hypoplastic. The pulmonary circulation is maintained either via a patent ductus arteriosus, or via collateral bronchial arteries, or both. The degree of dextroposition of the aorta likewise varies greatly. It may range from slight overriding to complete transposition of the great vessels, the aorta arising from the right ventricle and the pulmonary artery from the left ventricle. The hypertrophy of the right ventricle is merely the result of the combined effects of pulmonary artery stenosis, obstruction in the pulmonary circulation, and the shunt of blood flow. It does not constitute a congenital anomaly by itself.

Cyanosis exists from infancy and increases with age. The cyanosis is due to the venous arterial shunt into a dextroposed aorta. It depends mostly on the amount of blood reaching the lungs for oxygenation, as demonstrated by the work of Taussig and Blalock in 1947. These two factors obviously will be influenced by the degree of pulmonary stenosis, and hence the variation in the degree of cyanosis. Cyanosis may be observed late and only during some intercurrent illnesses. As cyanosis develops, clubbing of the fingers appears and it is proportional to the degree of cyanosis. Dyspnea likewise appears to be proportional to the severity of the anatomical defect. Helen Taussig observes that a child with tetralogy, when exhausted by exertion, assumes a squatting position. This has been observed in 75 per cent of the cases and no explanation is as yet available for the underlying mechanism of this phenomenon.

Epileptiform attacks are observed often in children with tetralogy of Fallot. Abbott considers that these attacks are due to combined effects of anoxemia and polycythemia, which might cause small areas of capillary thrombosis in the brain. Dextroposition of the aorta certainly favors the occurence of paradoxical embolism.

Polycythemia is a frequent phenomenon resulting from an effort to increase the oxygen-carrying capacity of the blood. Epistaxis, hemoptysis, and even hematemesis are commonly observed.

Enlargement of the heart is rather the exception than the rule. When present, it involves only the right ventricle. Many cases

show a smaller heart than normal. A systolic thrill may be present with the maximum intensity in the pulmonic area. A systolic murmur is present in a least 90 per cent of patients and it is most pronounced in the second and third left interspaces. However, the auscultatory findings are not pathognomonic.

Electrocardiogram shows right axis deviation of moderate or marked degree. Roengenogram of the chest quite often exhibits characteristic features, however by no means pathognomonic. Many cases show a cardiac silhouette of the "coeur-en-sabot" type, an abnormal projection of the aorta to the right, and a notable concavity at the site of the pulmonary artery segment. The apex is blunt and raised.

The upper mediastinal shadow may be quite narrow. Fluoroscopic examination in the LAO position shows a large pulmonary window and hypertrophy of the right ventricle. In the RAO position, the concavity of the pulmonary artery may become quite obvious. The hilar pulsations may be diminished or absent. The peripheral lung markings may be scant. Pulmonary congestion tends to exclude a diagnosis of tetrology.

Angiocardiography is of great value in tetralogy of Fallot. The type of pulmonary artery stenosis may be demonstrated. There is usually some delay in the filling of the pulmonary artery and a variation in the opacification dependent upon the severity of the stenosis. A shunt from right to left fills the dextroposed aorta within one-half seconds after the injection. The more equal the density of the contrast substance in the aorta and the right ventricle, the greater is the degree of the dextroposition or the transposition (Dotter and Steinberg). The scarcity of peripheral vascular markings may likewise be demonstrated.

Surgical correction so far as has been directed toward the improvement of the pulmonary circulation. The Blalock-Taussig operation consists of establishing an anastomosis between the side of the pulmonary artery and the left subclavian artery. Sometimes the carotid or innominate artery is used.

The Potts-Smith operation is a direct side to side anastomosis between the pulmonary artery and the aorta. Both operations intend to furnish more adequate blood to the pulmonary circulation. For further details the reader is referred to the original papers.

Although the congenital abnormalities still remain with the patient, the immediate effects of the operation are a great clinical improvement. Contra-indications to the operation are believed to be few: gross disturbance of conduction, evidence of bacterial endocarditis, renal disease, or recent cerebral accidents.

Case Report. Case III: D.A.R. #199-886. A nine year old white male had been cyanotic since birth and showed a marked retardation in growth and development. In addition, he had several episodes of syncope. Examination revealed a grade III systolic murmur best heard over the second left intercostal space and at the apex. This patient likewise showed clubbing of the fingers and toes. Hemoglobin: 18.5 gms. per cent. EKG revealed a right ventricular and a right auricular hypertrophy. Roentgenogram of the chest (Figure 3A) revealed a slightly enlarged cardiac silhouette with a concavity at the site of the pulmonary artery segment. Fluoroscopy revealed right ventricular hypertrophy. The appearance of the cardiac silhouette suggested a "coeur-en-sabot." Angiocardiogram was performed in the right anterior oblique position (Figures 3B and 3C) and showed an infundibular stenosis of the pulmonary artery. The aorta was densely opacified 1.5 seconds after the injection (Figures 3D and 3E), and situated anteriorly to the pulmonary artery, thus indicating a moderate degree of overriding and the presence of an interventricular septal defect. Cardiac catheterization showed right ventricular hypertension and a high inter-ventricular septal defect. An operation was performed and a Blalock-Taussig type of anastomosis between the left sub-clavian artery and pulmonary artery was established. When the patient was last seen, 10 months after the operation, his condition was markedly improved.

Interatrial Septal Defect

Interatrial septal defects constitute the most common of all congenital malformations of the heart. There are several types of interatrial septal defects. The more important are: (1) patent foramen ovale, (2)

persistent ostium primum, and (3) persistent ostium secundum. Blood may pass from one atrium to the other through this defect, the direction and the amount of shunt depending upon the difference in the pressure in the two chambers. Normally, the pressure in the left atrium is higher than that in the right, and blood will be shunted from left to right. This will markedly increase the amount of blood flow through the pulmonary circulation. Consequently, a greater load is put on the right ventricle. It hypertrophies and enlarges, the pulmonary vessels become enlarged and engorged. The left atrium, the left ventricle, and the aorta are normal or rather small in comparison with the right chambers and the dilated pulmonary artery.

The uncomplicated cases of interatrial septal defects may be entirely asymtomatic. Dyspnea is usually present and may be so habitual that the patient is not complaining of shortness of breath. It may manifest itself for the first time in the second or third decade. Cyanosis is inconstant and only noticable on exertion. It may become intense in failure. The cyanosis is due to a reversal of the shunt. These patients are otherwise pale and retarded in development.

Auscultation of the heart may reveal a systolic murmur at the apex or in the pulmonary area. However, in many cases, there is no murmur at all. The pulmonary second sound is accentuated, and a systolic thrill may be palpable at the same time.

Roentgenogram of the chest reveals an enlargement of the pulmonary artery segment and an enlargement of the cardiac silhouette. The pulmonary artery and its branches are enlarged and fluoroscopic examination reveals increased pulsation of these vessels at the hila, the socalled "hilar dance."

Electrocardiogram shows right axis deviation and a right bundle branch block. Auricular fibrillation occurs with some frequency.

Angiocardiography often reveals the fundamental hemodynamic abnormality. There is persistent opacification of the right atrium and a dilated right ventricle. Sometimes early opacification of the left auricle and simultaneous opacification of the right atrium can be demonstrated, thus indicating a shunt from right to left. The left ventricle and aorta are usually poorly outlined as to be expected.

Cardiac catheterization surpasses angiocardiography in the demonstration of interatrial septal defects. It reveals that the oxygen content of the blood in the right auricle is appreciably higher than of the blood from the superior or inferior vena cava.

Attempts to repair interatrial septal defects have been promising in the last few years and many patients all over the country have been successfully operated upon. Recent advances in anesthesia with the patient in a state of hibernation may open a new field for cardiac surgery.

Case Report. Case IV: A.D. #191-984.

A six-year old white female had a history of difficulty in breathing since the age of one. She also had frequent upper respiratory infections and was twice hospitalized for cardiac failure. The patient was well developed and well nourished. There was mild cyanosis of the extremities. Blood pressure: 112/68, pulse, 106/min. A loud, harsh, grade IV systolic murmur was heard at the second, third, and fourth interspaces on the left side, and transmitted to the back. Blood pressure and other laboratory tests were within normal limits. The electrocardiogram suggested a right and left ventricular hypertrophy as well as sinus tachycardia.

Roentgenogram of the chest (Figure 4A) revealed an enlargement of the cardiac silhouette with a prominent pulmonary artery segment and increased hilar vascular markings. Fluoroscopic examination revealed a moderate enlargement of the right ventricle and a "hilar dance."

Angiocardiography in the AP position confirmed the presence of the right ventricular enlargement, and the dilatation of the pulmonary artery segment (Figures 4B and 4C). In addition, it revealed reopacification of the right atrium and pulmonary vessels (Figures 4D and 4E) after opacification of the aorta, highly suggestion of interatrial septal defect.

Cardiac catheterization was carried out, and the findings were inconclusively mostly due to technical difficulties. The child has been followed in the pediatric clinic and surgical repair of the defect may eventually be considered.

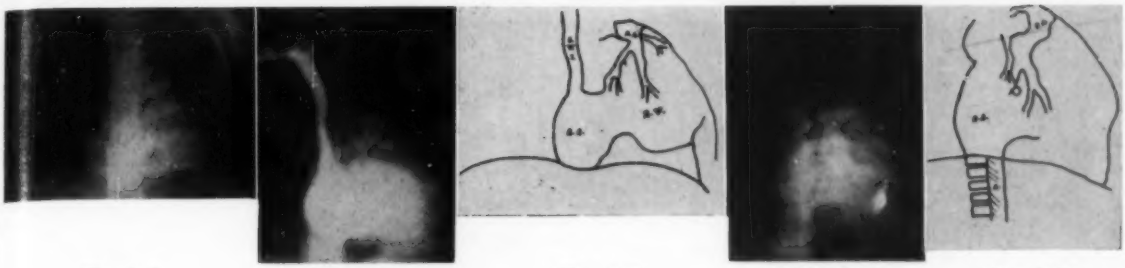

Fig. 4 A Fig. 4 B Fig. 4 C Fig. 4 D Fig. 4 E

Patent Ductus Arteriosus

A persistent patent ductus arteriosus allows a shunt of blood from the aorta to the pulmonary artery, the pressure normally being greater in the left side of the heart than that in the right side. A large shunt results in a low diastolic pressure and is not only a cause of increased work by the left ventricle, but also puts a greater load on the work of the right ventricle. The pulmonary artery and its branches become dilated. The children with a patent ductus arteriosus, particularly those with a large shunt, are pale and underdeveloped. Cyanosis is absent at rest, but it may appear on exertion. In certain rare cases of long duration, the pulmonary pressure may increase to such a degree that it is equaled or exceeds the aortic pressure, thus reversing the direction of the shunt in the patent ductus and giving rise to late cyanosis of "cyanose tardive."

Symptoms are occasionally present and are usually those of dyspnea on exertion, and easy fatigability. A characteristic machinery or continuous murmur is best heard in the second left interspace close to the sternum and is usually diagnostic of a patent ductus. However, many cases do not present the typical murmur, particularly children under the age of three. Undoubtedly, a patent ductus may be present in the absence of a machinery murmur. The pulse pressure is often increased, the diastolic pressure being lower than normal.

The electrocardiogram is usually within normal limits. There may be a tendency to left axis deviation if the shunt is large. Roentgenograms reveal only slight enlargement of the cardiac silhouette and fluoroscopy demonstrates biventricular cardiac enlargement as well as an enlargement and an expansile pulsation of the pulmonary arteries.

Angiocardiography may give additional evidence but is rarely indicated in the presence of a typical clinical picture. It may exclude or confirm the presence of a suspected associated malformation. A dilatation of the aorta distal to the origin of the left subclavian artery may be suspicious of a patent ductus. (Steinberg, Grishman, Dotter, Sussman). Angiocardiography may show the enlargement of the pulmonary artery and an elevation of its left main branch. A disturbance in the hemodynamics may be presumptive of a diagnosis of a patent ductus arteriosus. The left pulmonary artery and its branches may be reopacified at the time of the opacification of the aorta, denoting a shunt between the aorta and pulmonary artery. Retrograde aortography will occasionally demonstrate the patent ductus.

Surgical correction consists of ligation of the patent ductus arteriosus. The diastolic pressure rises, the pulse pressure becomes normal, the size of the heart diminishes, and the murmur disappears. If operated at an early age, the tendency to underdevelopment

Fig. 5 A Fig. 5 B Fig. 5 C Fig. 5 D Fig. 5 E

may be checked. It certainly tends to prevent the occurrence of congestive failure and diminishes the risks of infectious endocarditis, a quite common accompaniment of a patent ductus arteriosus.

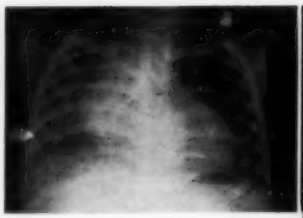

Fig. 6 A

Fig. 6 B

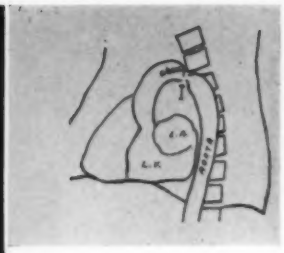

Fig. 6 C

Case Report. Case V: K.S.H. #189-472.

A three-year old white female had frequent upper respiratory infections, easy fatigability and a slow development. There was no cyanosis. A continuous grade IV murmur was heard over the first and second intercostal spaces. A grade II systolic murmur was heard over the apex. EKG showed a suggestion of left ventricular hypertrophy. Roentgenogram of the chest (Figure 5A) revealed a slight enlargement of the cardiac silhouette with a straightening of the left ventricular border suggestion of left ventricular enlargement. There was increased vascularity of the lungs. Fluoroscopy confirmed the above mentioned findings. Angiocardiogram in the LAO position (Figures 5B, 5C, 5D, and 5E) revealed a persistent reopacification of the left atrium and left ventricle, and reopacification of the branches of the pulmonary arteries, indicating a shunt between the aorta and the pulmonary artery (patent ductus arteriosus). The patient was operated on and the patent ductus was ligated. The patient was seen 15 months after the operation and showed a satisfactory progressive course and clinical improvement.

Coarctation of the Aorta

Coarctation of the aorta is a congenital narrowing of the arch of the aorta. Two types are commonly distinguished: (1) The "infantile type," in which the narrowing is at a site proximal to the left subclavian artery. Blood supply to the lower extremities and trunk usually occurs via a patent ductus arteriosus. Hence, there is a selective cyanosis of the lower extremities and trunk. Patients with this type of coarctation usually do not survive infancy. (2) The "adult type," where the stenosis is distal to the origin of the subclavian artery, and at, or adjacent to, the site of insertion of the ductus arteriosus.

Coarctation of the aorta may be entirely latent and unsuspected during life. However, the great majority of the patients sooner or later do develop a typical clinical picture.

Symptoms are uncommon in childhood. These may consist of recurrent epistaxis, exertional dyspnea, and very occasionally subarachnoid hemorrhage. Symptoms most often appear in early adult life: palpitation, dyspnea, headaches, tinnitus, pulsations in the neck, head nodding with systole, etc. These phenomena are the results of a hypertension in the upper parts of the body. The lower extremities are cold, numb, and pale, as a result of diminished vascular supply. There is hypertension in the upper extremities and hypotension or unobtainable blood pressure in the legs. The femoral pulse is absent or hardly perceptible. Uncomplicated cases of coarctation of the aorta do not show cyanosis.

The heart may be normal in size or slightly enlarged. A systolic murmur may be heard, loudest at the base of the heart. The murmur is heard over the back, particularly well over the scapulary vessels. Electrocardiogram usually shows left ventricular hypertrophy.

Roentgenogram of the chest may substantially supplement the clinical findings. Notching on the inferior surfaces of the posterior extremities of the third to the ninth ribs is commonly observed. The notching is due to pressure atrophy by dilated tortuous intercostal vessels as a result of an increased collateral circulation. The cardiac silhouette may show slight enlargement with an accentuation of the left ventricular border.

Angiocardiography is of paramount importance in coarctation of the aorta. It usually demonstrates the actual site and the extent of the coarctated segment. The ascending aorta is usually dilated while the transverse arch appears somewhat narrowed and elongated. The left subclavian artery is usually dilated, and the coartation is distal to its origin. The aorta distally to the coarctation quite often shows a bulging comparable with the "post-stenotic dilatation" of the pulmonary artery seen in isolated pulmonary valvular stenosis.

Occasionally, angiocardiography may fail to demonstrate the site of the coarctation, and retrograde aortography may be applied. This method offers more detailed information and better visualization of the aorta and its branches. It consists of an injection of the same contrast medium, however, in a lesser concentration (Urokon-Sodium 30 per cent), into the brachial or common carotid artery in a retrograde manner. This diagnostic procedure is more elaborate and should only be applied when direct angiocardiography fails to demonstrate the coarctation.

Surgical correction aims toward an excision of the narrowed segment and an establishment of an end to end anastomosis (Gross).

The results of the operation are impressive. The pressure in the upper extremities falls, and rises in the legs. The collateral vessels decrease in size gradually, and the risks of infectious endocarditis are greatly diminished.

Case Report. Case VI: M.L.R. #198-090.

A four-year old colored female showed a severe degree of anaemia and marked underdevelopment. The patient had recurrent episodes of epistaxis. The blood pressure was 156/70 in the left arm, and 162/70 in the right arm. The blood pressure in the legs was unobtainable. A gallop rhythm and a systolic murmur were heard over the entire precordium with the maximum intensity over the third intercostal space. Hemoglobin was 3.0 mgs. per cent. EKG showed a partial heart block. Roentgenogram of the chest (Figure 6A) revealed an enlargement of the cardiac silhouette. The right para-mediastinal shadow probably represents an enlarged right lobe of the thymus. Angiocardiogram in extreme left anterior oblique position (Figures 6B and 6C) revealed an interruption in the outline of the aorta immediately distally to the left subclavian artery, denoting the coarctation of the aorta.

Case Report. Case VII: D.R.P. #174-730.

A four and one-half-year old white male with congenital hypospadia and stenosis of the urinary meatus, was suffering from frequent upper repiratory infections and easy fatigability. No cyanosis was present. The blood pressure in the arms was 130/84. The femoral pulses were weak, the popliteal and the dorsalis pedis pulses could not be obtained. The blood pressure in the legs was not obtainable. A grade III soft blowing systolic murmur was heard over the entire precordium with the maximum intensity over the aortic and pulmonary areas. EKG revealed a partial heart block. Roentgenogram of the chest (Figure 7A) revealed a slight enlargement of the cardiac silhouette. There was widening of the superior mediastinum and an increased vascularity in the hilar areas. An angiocardiogram was performed in the AP position (Figures 7B and 7C) and a double superior vena cava was outlined, the right one opening into the right auricle, the left one opening into the left auricle. The coarctation of the aorta was not demonstrated at this time.

A retrograde aortogram was performed. The contrast medium was injected into the left brachial artery. The aorta and its

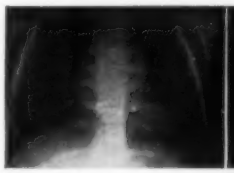

Fig. 7 A

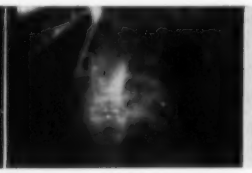

Fig. 7 B

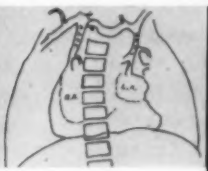

Fig. 7 C

Fig. 7 D

Fig. 7 E

branches were well demonstrated (Figures 7D and 7E) and the coarctation of the aorta, distal to the left subclavian artery was outlined.

Summary

Angiocardiography has become an essential part of the standard clinical investigative procedures of cardio-vascular diseases. This method has been extremely valuable in the determination of congenital malformations of the heart. Accumulated experience has indicated the values as well as the shortcomings and limitations of this diagnostic method. The interpretation of angiocardiograms has to be correlated closely with the clinical picture and with all other available methods, in particular with cardiac catheterization. These two methods, angiocardiography and cardiac catheterization, supplement each other and ought to be applied in all suspected cases in order to gain supplementary information, in order to visualize the suspected defect, and, in order to demonstrate associated defects that might not have been suspected by other investigative methods.

Discussion of congenital malformations of the heart is no longer an academic problem. A great number of these patients can be helped by cardiac surgery, and an accurate pre-operative diagnosis is of paramount importance.

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Medical Grand Rounds

INFLUENZA *and* FLU

STEWART WOLF, M.D.

Stewart Wolf M.D.: Today we are considering a very timely subject. A good many of our staff and their families have been laid up with self-limiting illnesses variously called flu, virus, a bad cold or intestinal flu. Doctor Robert Bird will tell us of the first patient.

Robert Bird M.D.: The first case is that of a 30-year-old resident physician who was taken acutely ill September 22, 1954. His past history was unremarkable. On September 22 he had a mild diarrhea which lasted during the morning and was unassociated with much abdominal distress. For the remainder of the day he worked and felt essentially well. Late that evening he was awakened twice with shaking chills. On arising on the morning of the 23rd, his temperature was 101.4. He had a generalized headache, severe lower dorsal and lumbar backache, and anorexia. During the day of the 23rd he continued on duty though feeling very much below par. On September 24 he had less fever and less diarrhea but headache was more intense and in addition he had pains in the knees and other large joints. He had taken no medications except aspirin. On the 24th his physical examination was entirely unremarkable except for slight fever and moderate photophobia. The fundi, ears, nose and pharynx were all clear. There was no generalized or localized lymphadenopathy. Examination of the heart and lungs and abdomen were all within the limits of normal. A white count was 12,700 with a differential of 73 per cent adult polys, 5 per cent bands, 11 per cent lymphocytes, 8 per per cent monocytes, and three per cent eosinophiles. Symptomatic therapy was continued. By the 27th the patient felt entirely

well and was back at work on a full schedule. One week after the onset of the illness, there was a relapse of malaise, aching of the back muscles and joints, and diarrhea which lasted for one day. The patient was not examined at this time. Subsequently he has been entirely well.

This history is fairly representative of a significant number of the hospital staff who during recent weeks have been similarly ill. Some of the patients have shown more respiratory symptoms, manifested by lacrimation, suffusion of the conjunctivae, and a great deal of coughing, sneezing and rhinorrhea. Still other individuals have shown more headache and quite a few have developed actual nuchal rigidity. A marked somnolence in some patients has been out of proportion to the degree of fever or other evidence of disability.

Ted Clemens M.D.: This is the case history of a 29 year old licensed practical nurse who noted lacrimation, rhinorrhea and conjunctivitis followed in four-six hours by mild stiffness of the neck, chills, and fever. The next day she had six-eight loose green bowel movements, general malaise, myalgia, and her neck remained stiff. Symptomatic therapy was instituted, but on the third day of her illness she noted a shaking chill followed by a fever of 104 degrees, many loose stools, generalized throbbing headache, and continuation of the earlier symptoms. She was seen in the Emergency Room where physical examination revealed her to be acutely ill with temperature of 101 degrees. There was marked lacrimation, photophobia, and moderate conjunctivitis. The pharynx was diffusely injected. Flexion of the neck was painful. Urinalysis was normal and there was a moderate leukocytosis with shift to the left. Cerebrospinal fluid examination revealed 30 mg. per cent protein, no cells, normal sugar and chlorides. Culture of the cerebrospinal fluid was sterile. Chext x-ray was normal. She was treated symptomatically with salicylates, codeine, phenobarbital, and kaopectate for the diarrhea. Temperature was normal on the second day after admission, although neck stiffness and headache persisted. By the third hospital day she was asymptomatic. She was discharged asymptomatic after five days of hospitalization and returned to work three days later. Serum drawn during the illness and sent to the State Health laboratory for complement fixation test for viral infections revealed positive titers of 1:16 for influenza type A, PR8 strain. Complement fixation for other viral infections was negative save for 1:16 titer to the mumps antigen.[1]

Mark Johnson M.D.: The third patient is a 22-year-old male medical student who was well until 2 a.m., October 12, 1954, at which time he awoke from a sound sleep suffering with a generalized headache. Upon arising he experienced profound nausea and during the ensuing 12 hours he vomited 7 or 8 times. The vomitus gradually changed in content from undigested food matter to small quantities of mucoid material, sometimes flecked with blood. Frequent bowel movements marked the early onset of symptoms, so that initially the picture was that of an acute gastroenteritis. He was seen in the Health Service Clinic on the afternoon of October 12, 1954, where he was found to have a temperature elevation to 100 degrees Fahrenheit, a moderately injected pharynx, slight diffuse upper abdominal tenderness, and increased peristaltic sounds over the abdomen. He was given emetrol and was advised to return home to bed rest and to employ simple supportive measures. Although the diffuse headache and generalized malaise persisted, the symptoms of gastrointestinal disturbance subsided for approximately 30 hours, until the evening of October 13, 1954, when the nausea and vomiting returned. This time it was accompanied by a generalized myalgia, a persistent chilly sensation, increased severity of the headache, and a sensation described as "giddiness and light-headedness". He began to feel feverish for the first time and the patient spent a generally restless night prior to his return to the hospital and subsequent admission on the morning of October 14, 1954.

The past history contained no pertinent points and a careful attempt to establish a cause for gastroenteritis was unrewarding.

Physical examination disclosed a young white male who appeared to be acutely ill and slightly obtunded; however, he was well oriented and cooperative. The oral tempera-

1. Serum from the second patient drawn 4 weeks after the initial specimen showed complement fixation titers of 1:64 for both the FM1 and PR8 strains of type A influenza and 1:16 for Type B, Lee strain.

ture was 103.6, pulse rate 120, respirations 20, BP 160-80. Both ear drums showed linear streaks of hyperemia. The conjunctivae and corneae were slightly suffused. The nasal mucosa was dry and reddened. A mild malar flush was apparent on the face and associated with perioral pallor, dry lips, and an offensive breath. Mucosa of the posterior pharynx and soft palate was lightly reddened and somewhat edematous. No significant lymphadenopathy were present. There was a moderate degree of generalized abdominal tenderness but bowel sounds were normal. Superficial and deep reflexes were normal. There was no nuchal rigidity, and the Kernig and Brudzinski signs were not present. Admission laboratory studies revealed the urine to be normal and the white blood count to be 18,600 with 79 per cent neutrophils, 16 per cent lymphocytes, and five per cent monocytes. The admission diagnosis was viral infection, type undetermined. The patient was placed at bed rest and was given parenteral fluids and aspirin compound tablets for symptomatic relief. On the day following admission, a moderate degree of confusion and disorientation was apparent and definite nuchal rigidity had appeared. Fever remained high. Cerebrospinal fluid contained 110 white blood cells, all of which were lymphocytes, and 50 mg. per cent of protein. The spinal fluid was negative for organisms by smear and subsequently by culture, and blood cultures were negative. Symptomatic therapy was continued and by the fourth hospital day the patient showed definite improvement. He was discharged to resume classes after nine days of hospitalization. Complement fixation titers on serum drawn during the acute stage of his illness were 1:8 for influenza type A, strains FM1 and PR8, and for type B, Lee strain. There was a 1:16 titer for mumps. Tests were negative for lymphocytic choriomeningitis, the equine encephalomyelitides, St. Louis encephalitis, and Q fever.

Clair Liebrand M.D.: This 22-year-old white male was referred from one of the state corrective institutions on October 7, 1954, with the referring diagnosis of meningitis. According to available history, he was noted to be listless by his fellow inmates for a period of approximately one week prior to his admission to University Hospital. Two days prior to admission he reported to sick bay at the reformatory complaining of severe headache. Because of a stiff neck, a diagnosis of early meningitis was made and the patient was started on sulfadiazine, penicillin, streptomycin and achromycin. Two days later, due to persistent symptoms and progressive stupor, a lumbar puncture was done and was said to show 300 white blood cells, type not stated, and gram positive cocci on smear. The patient was referred to University Hospital where examination in the Emergency Room revealed a comatose, dehydrated white male whose fever was 108.7°. Pulse was 120, respirations 36 and Cheyne-Stokes, and blood pressure 115-50. There were defisite signs of meningeal irritation. The upper respiratory tract, the heart, lungs, abdomen and the lymphatic system were unremarkable. The patient was sent immediately to the ward with the diagnosis of acute meningitis.

Physical examination upon arrival on the ward was unchanged save for lowering of the body temperature to 105°. A lumbar puncture was done immediately and yielded slightly opalescent fluid under normal pressure. Cell count on the fluid revealed 165 white blood cells, of which 13 were adult neutrophils and 152 lymphs. Protein was 75 mg. per cent and sugar 78 mg. per cent. No organisms were seen on smears, nor were torula demonstrable in India ink preparations. The urinalysis was normal save for a trace of protein. White blood count on admission was 12,500 with 43 per cent polys, 48 per cent lymphocytes, seven percent monocytes, one per cent eosinophils, and one per cent basophils. Serum electrolytes were normal. Nasopharyngeal culture revealed hemolytic staphylococcus aureus, and blood cultures were negative, as were all cerebrospinal fluid cultures. The patient was treated with parenteral fluids and other supportive measures, and because the gram positive cocci reported in the spinal fluid smear prior to admission, he was continued on penicillin, 1,000,000 units every two hours, and intravenous sulfadiazine. In spite of ther-

2. Convalescent titers for the third patient were 1:16 for influenza type A, strains FM1 and PR8, and for type B, Lee strain. The titer to mumps also was reported as increased to 1:32, exemplifying the importance of significant rises rather than merely changing titers.

apy his course was progressively downhill, although his fever gradually diminished. Daily lumbar taps revealed no significant change from the initial spinal fluid findings. On the fifth hospital day while being turned to his side for spinal puncture, he became cyanotic and a tracheotomy was necessary. Subsequent to this his respirations became progressively more labored, and he expired October 12, 1954. Autopsy revealed an edematous, congested, inflamed brain with cerebellar pressure cone. In addition severe purulent tracheobronchitis, petechial and ecchymotic hemorrhages of the gastrointestinal mucosa, moderate congestion of the viscera, and moderate parenchymatous degeration of the heart, liver and kidneys were present. Subsequent to death, reports on serum sent to the State laboratory were negative for lymphocytic choriomeningitis, eastern and western equine encephalitis, St. Louis encephalitis, mumps, and Q fever. Complement fixations for influenza were not done on this specimen. Serum drawn on the day of death showed a titer of 1:4 for lymphocytic choriomeningitis; and for the influenza viruses, 1:16 for type A FM1 strain; 1:8 for type A PR8 strain; and negative for B, Lee strain.[3]

Doctor Wolf: We have heard four patients presented to us with symptomatology and findings on physical examination and laboratory studies which we are inclined to call influenza or "flu". It is striking that in this group of conditions we do not see a stereotyped picture, but rather a variety of symptoms including headache, rhinorrhea, sore throat, cough, aches and pains throughout the entire body, fever, diarrhea, nausea, and vomiting. Fever and aching may be the first symptoms or symptoms suggestive of the common cold. Another patient may wake up suddenly with nausea and vomiting, while symptoms in some patients may be limited to diarrhea. Certainly we are not seeing a clear-cut, single syndrome. Some patients in the current outbreak have noted heartburn, epigastric pain, or symptoms of cardiospasm. Also striking is the frequency with which leukocytosis was reported and how frequently we have seen such symptoms as stiff neck, insomnia, disorientation, etc. These cases give rise to a number of questions: In particular, we are dealing with one disease only? Is this picture due to a single virus which manifests itself differently in different individuals? Is there a predictable difference in the clinical picture of different strains of virus? How reliable are our diagnostic tools, and how do we interpret them? We also are interested in the questions of immunization and therapy. Are vaccines of any value? What do antibiotics accomplish? Doctor Scott, would you open the discussion and tell us something about the viruses which cause symptoms such as these, especially the influenza viruses?

Vernon Scott Sc.D.: There are three totally unrelated immunological types of influenza virus that produce the same symptomatology in man. The first is type A and is comprised of many strains. Type A influenza was first isolated by Smith, Laidlaw, and Andrewes in 1933. In 1934 Francis isolated the PR8 strain of influenza which is the classical type A known here in the United States. There have been several A strains isolated since 1934, but the PR 8 has the broadest antigenic base of any of the type A influenza viruses isolated so far. Now in 1947 there was a new type A virus going around which differed from the A virus isolated heretofore, but it was immunologically related to the A type and was, therefore, designated as A'. Every year since 1947 there has been at least one and sometimes several new A' strains isolated in the United States. The second type of influenza virus, the type B, includes the Lee strain virus which was the first of the strains isolated (1940) and has the broadest antigenic base of any of the B types. Since that time many

3. Histological study of the brain was described by Dr. Walter Joel as follows:

Slides from the hypothalamus show extensive lymphocytic cuffing of the blood vessels. Areas of ring bleeding are seen in the Virchow-Robin spaces. There are many areas of demyelinized tissue, especially around vessels, and some areas not related to vessels show proliferation of oligodendroglia and lymphocytes.

In the pons there are perivascular infiltrations as previously described, although degenerative changes are less marked. Some areas show degeneration of the ganglion cells with cytolytosis; some ganglia show only cytoplasm without nuclei; and some present clumping of the Nissel substance. The distribution of major involvement in the pons is in the pedunculi and tegmentum.

The cerebellum and cerebral cortex show centers of degeneration and cuffing as described elsewhere, though less marked. The cortical and pial vessels are dilated and filled with blood, and the meninges show increased numbers of lymphocytes.

The picture is typical of encephalitis, and compatible with St. Louis or eastern equine encephalitis, though in the latter cyst formation is often prominent. It is impossible to make a type diagnosis from the histological picture.

type B strains have been isolated, and all of the B strains are immunologically related. All the A strains are similarly immunologically related, but the A strains are not related immunologically to the B strains. In 1949 Dr. R. M. Taylor of the Rockefeller Institute isolated a new type of influenza virus known as the C virus, and since that time this virus has been isolated by several workers and has been shown to be widespread. It is immunologically distinct from the A and B types of influenza virus.

Dr. Wolf asked if there was a difference in the diseases which these viruses produce. Clinically one cannot distinguish between the disease patterns produced by type A or type B. In general the disease produced by the A influenza virus is more severe than the disease produced by the type B virus but both types may produce diseases ranging from severe illness down to subclinical cases. Immunological procedures have demonstrated that such subclinical cases of influenza do occur. The information on type C viruses is still limited, but they appear mainly to produce low grade infections with predominantly upper respiratory symptoms.

How does one make the laboratory diagnosis of influenza? The etiologic diagnosis can be made in two ways. One way is the isolation of the virus and its subsequent identification. The virus is isolated from nasal washings or throat gargle specimens taken during the first 24 to 48 hours of the disease. (The sooner the specimen is taken, the more likely one is to isolate the virus.) These specimens are mixed with suitable antibiotics, such as penicillin and streptomycin, and inoculated into the amniotic cavity of the developing chick embryo. After a suitable incubation period the viruses are harvested and their presence is detected by their ability to agglutinate the erythrocytes of humans, guinea pigs, or chickens. After the virus has been isolated, it is identified using immunological procedures with known immune sera. The immunological procedure usually used is the hemagglutination inhibition test; however, there are others that are useful, namely the complement fixation test, the in vivo neutralization test, and the protection tests. The second method for the laboratory diagnosis of influenza is the use of immunological procedures employing acute and convalescent sera. It is very important that paired sera be obtained. I know of no laboratory that will make a diagnosis of influenza on a single serum specimen. Not only is it important that both acute and convalescent serum be used, but there must be a four-fold rise in antibody titer between the titers of the two specimens before it is diagnostic. The reason one cannot give a diagnosis on one specimen alone is that everyone five years old or older has at some time had influenza, and Rickard in 1941 and many others since then have shown that everybody has a residual influenza antibody titer. This residual titer often may range as high as 64 and occasionally to 256, and therefore the single titer is not diagnostic. A four-fold increase is needed to differentiate the residual from the newly acquired titer. The acute serum specimen should be taken at the onset of the disease when the patient first comes to the doctor. The second serum specimen should not be taken before a two week interval has elapsed. It has been shown by many workers that the antibodies to influenza begin to appear around the tenth day and reach their peak titer around the fourth to the sixth week, remain steady for a short time, and then begin to wane. A person then who has had an attack may be susceptible again within eight months or a year because of the loss of protective antibodies. I can't emphasize too much the value of paired specimens (acute and convalescent serum) in the serological diagnosis of influenza or any other viral infection. Laboratories should not do immunological tests on one serum specimen; the information obtained is valueless.

Now as to Doctor Wolf's question regarding vaccination. There is a vaccine for the prevention of the disease influenza. The biological houses put out a vaccine every year which is effective against the viruses that are included in that vaccine. The main trouble with the vaccine is that it may not contain the strain of influenza virus that is prevalent in the expected epidemic. For instance, in 1944 the vaccine which was used protected against the current influenza epidemic. In 1946 the vaccine protected against

the type B influenza outbreak, but in 1947 people might just as well not have been vaccinated because it was that year that the A' strain, FM1, appeared, and since that time many mutants of the A' strain have been appearing. This pesky influenza virus is probably the worst of all the viruses known to man from the standpoint of mutation. What biological houses try to do each year is to include the broadest antigenic virus of the A type and the B type and one or two of the viruses that were prevalent the last season. You can see the difficulties involved. The vaccine may not contain the proper antigens to stimulate the host to produce protective antibodies. It must be given at least two weeks prior to exposure since it takes at least ten days for demonstrable antibodies to be developed. The influenza vaccine is made from the allantoic fluid of the chick embryo, is concentrated and partially purified, then inactivated by chemicals or ultraviolet light. If the vaccine used includes antigens of the particular strain which comes along and is given far enough in advance of exposure, then temporary protection is achieved. This probably is effective for only about three months but that is enough to get one through the winter.

Epidemics of influenza are always interesting. Outbreaks of influenza A seem to go in cycles of two or three years, while the disease produced by the type B viruses seems to go in cycles of four to five years. Great pandemics, world-wide in extent, sweep the world at intervals of 20 years or more. Between pandemics the disease is universally endemic, and from time to time localized epidemics occur. They start from a definite geographic focus and spread rapidly. A localized epidemic lasts only three to six weeks, is less severe than pandemic influenza, and has a lower attack rate. When a pandemic occurs, it is composed of three distinct waves separated by months or a year. There is an outbreak in progress somewhere in the world all the time. We know that the highest percentage of cases is usually in the winter or early spring, although there may be some cases in the late fall. It was the type B virus that was making the rounds last year. An outbreak of B influenza appeared in California. It was first discovered in January in Santa Clara County, and February, March and April it went throughout California. In March it was isolated and studied in an outbreak in the Navy in Illinois, and in the course of the season many spots in the United States reported outbreaks. During this period some C strain viruses were also isolated, however, the period from July, 1953, through June, 1954, was noted for the fact that it had the lowest ebb of influenza in years. This year they are expecting an A influenza epidemic. The first reason for believing that it will be this type is that there were no type A viruses isolated last year, and this virus goes in two-three year cycles. The second reason is that in May and June of this year workers in South Africa isolated the type A influenza virus. The strain isolated there is being studied in the World Health Organization office in London at the present time. At about the same time there were several sharp outbreaks of this A virus in Australia, May and June being their winter. Since August there have been many short outbreaks in the Philippine Islands. The World Health Organization study groups are watching these epidemics very closely. In the United States at the present time there are over 50 laboratories collaborating with the World Health Organization influenza program to describe the epidemic, to isolate the viruses, and to aid in the diagnosis of influenza.

Where is the interepidemic habitat of influenza virus? Influenze virus has been demonstrated to be present in populations during interepidemic periods. This may be the time when many of the subclinical cases are going on, but sporadic cases of influenza occur also. Doctors see them but may not recognize them apart from other acute respiratory diseases, since the disease is hard to differentiate clinically from many other acute respiratory diseases until it becoms epidemic; therefore not until its incidence increases sharply do doctors begin to diagnose it clinically. A second explanation of the interepidemic habitat is the fact that there is an epidemic of influenza in progress somewhere in the world all the time. Thus with our fast means of transportation and our loss of protective antibodies within six months of recovery from a former attack, we find the scourge of influenza with us every winter.

Dr. Thomas H. Haight: The clinical diagnosis of influenza is very difficult. During interepidemic periods there are no distinguishing clinical features separating the disease from certain other viral infections or certain bacterial respiratory infections. During the epidemic periods, it is not so difficult. Although an occasional epidemic may occur earlier, it is rare to find influenzal infections much before about Thanksgiving. The major epidemics rarely get going before December or much later than late February or early March. A typical case of influenza comes on abruptly, often with shaking chills and high fever, and is usually accompanied by a considerable amount of aching, including the head, the muscles, and the eyes. The fever ordinarily ranges between 100 and 104 degrees. The patient is likely to be apathetic, with suffused face and injected conjunctivae. Symptoms are otherwise primarily of the respiratory system, with coryza, mild sore throat, substernal soreness and a cough which is usually nonproductive. Physical findings are generally unremarkable, although occasionally one sees purplish discoloration of the posterior pharynx. The leukocyte count may be slightly increased initially but a normal count or leukopenia is the rule. Nasopharyngeal cultures show a normal flora and blood cultures are negative. The usual duration is two-three days in a mild case. A longer duration suggests a complication, as does persistent leukocytosis, and the most common serious complication, as does persistent leukocytosis, and the most common serious complication is staphyloccocal pneumonia. There is no specific therapy for influenza; the disease is self-limiting, and antibiotics are indicated only for a specific complication or to prevent secondary complications, particularly in young children or elderly people or in patients who have other complicating diseases, particularly of the lungs.

Now do any of these cases presented today illustrate the picture of true influenza? I don't think so. Certainly the first and third patients fit no known pattern of influenza. There is, of course, the time honored diagnosis of intestinal flu, but we have come to recognize that this word "flu" is a misnomer in this instance. None of the influenza viruses has ever been isolated from patients suffering from such gastrointestinal illnesses in spite of repeated efforts in major laboratories in the country. These gastrointestinal illnesses which tend to occur occasionally in epidemic form are probably viral infections, but not influenza. Doctor Jordan and associates in Cleveland succeeded in isolating two filterable agents from the stools of patients with similar symptomatology. Further, they were able to prove that the filterable agents, presumably viruses, could reproduce the same disease pattern when given to healthy volunteers. Our second patient whose main complaints were systemic in origin and who did appear to have some degree of pharyngitis, probably represents another type of viral infection. During World War II, the Army Epidemiology Board had as one of its commissions the Commission of Acute Respiratory Diseases. One of their main problems was to study the frequent and recurrent epidemics of presumptively nonbacterial respiratory infections as they occurred, particularly in military populations. They became impressed with certain variations in the pattern of respiratory tract infection in military populations when contrasted with civilian populations, and the entity ARD (for Acute Respiratory Disease of new recurits) was thought for some time to be specific virus syndrome. It is now quite obvious that ARD is not an entity, but rather there are many other virus infections of the respiratory tract which we are just beginning to understand. Through the use of newer techniques in the laboratories, such as tissue cultures, the use of HeLa cells in tissue culture, and improved serological methods, new viruses are constantly being isolated. Many of these cannot be causally related to infection, but some of them have been found to be so related. Doctor Hilleman at the Army Medical Service Graduate School in Washington, and Doctors Rowe and Heubner of the National Institutes of Health and Doctor Ward of Johns Hopkins have recently isolated such viruses and have shown specific serological evidence of increasing antibody titers to these new viruses. The exact role which these new cytopathogenic agents play in the frequent com-

mon cold-like or other similar mild epidemic respiratory infections needs considerable clarification. We are really just on the brink of this field at the present time. It would appear that the diagnosis of the fourth patient must await the final pathological report, since further serological examinations for the virus encephalitides will be impossible due to the patient's death. There is surely nothing inconsistent with lymphocytic choriomeningitis, nor however, with many other conditions which we need not discuss now.

I am very glad that Doctor Scott has emphasized to you the importance of understanding the results of influenzal serology. One of the commonest failings is to accept a single report showing influenzal antibodies to any of the virus strains as being diagnostic. Actually some of these titers which we have just seen are below what one might expect to find in the population at large, and therefore the serological diagnosis of influenza must absolutely depend on demonstration of a fourfold or greater rise in titer between an acute and a convalescent blood specimen over a minimum of ten days to two weeks. Amazingly enough, even with serial serum studies the laboratory proof of the clinical diagnosis is very hard to come by. We had the opportunity to observe several epidemics of influenza at the Great Lakes Naval Training Center and accumulated a sizable series of patients on whom we had fairly comprehensive information. When we excluded the obvious bacterial infections which occurred during influenza epidemics, it was surprising to find that in this large group of patients whose symptomatology was identical, we could establish a laboratory diagnosis in only one third of the patients by either virus isolation or significant rises in antibody titer. So you see, we have no clear-cut clinical grounds nor indeed any highly sensitive laboratory tests which will enable us to prove the diagnosis of every case of influenza. Dr. Jonas Salk has even postulated there may be some relationship between influenza epidemics and epidemics of other virus infections, and this perhaps may account for the fact that we can prove serologically or by virus isolation only one third of the cases of influenza during an epidemic period. It will take several years for us to understand this better. The problem of using rises in antibody titer as evidence of influenza virus infection is well illustrated by a study of 208 patients with scarlet fever which we made a couple of years ago. It just happened that we were observing these patients with scarlet fever during the same time that an explosive outbreak of influenza occurred on the base, and being interested in surveying these patients, we ran influenzal antibody titers on them too. To our great surprise, we found that 22 per cent of them showed significant rises to influenza virus of the prototype strain. In other words, these patients who were sick with scarlet fever but who presented no further evidence of any other infection had produced antibodies to the influenza virus which was present on the base at the same time. Whether these were truly asymptomatic infections or whether the scarlet fever masked a mild sub-clinical case of influenza is hard to prove, but it does point out some of the difficulties in laboratory diagnosis.

Dr. Harold Muchmore: Would Doctor Scott say something about the use of adjuvants in vaccines? The entire U. S. military population was to have been immunized by October 15 this year with a vaccine for which great hopes were held, partly because of the adjuvant it contained.

Doctor Scott: Adjuvants are agents added to the vaccine to delay the metabolic breakdown of the antigen and to prolong its stimulus to antibody formation. Perhaps the most commonly used agent is mineral oil.

Doctor Wolf: What percentage of people can be successfully immunized against influenza?

Doctor Scott: Probably about 85 per cent. Some people are just poor antibody producers, and as we have said, the various strains differ in their antigenicity.

Doctor Haight: Doctor Scott has already mentioned the temporary nature of the immunity the vaccines produce. This is a point worth emphasizing a bit, for there is an important immunological principle involved. The vaccines employing living organisms such as vaccinia for smallpox or Theiler's vaccine for yellow fever confer a degree of immunity comparable to the natural infection. Vaccines containing inactivated organ-

isms fail to do this; hence the need for recurrent vaccination to protect against influenza or poliomyelitis, among many others. The problem of protection against influenza is far from solved, so in the meantime we can only hope there is sufficient antigenic relationship between the vaccine and the prototype strain to afford protection against the expected epidemic.

Doctor Wolf: Should we attempt to isolate patients such as these we have presented today?

Dr. Scott: Isolation is not feasible. These diseases are usually spread by droplet infection, with the respiratory tract the usual portal of entry. Healthy carriers as well as patients probably spread the disease, and generally the patient will have passed the most infectious stage when the diagnosis is made.

Dr. Haight: As a general policy, patients such as our fourth case are isolated in most hospitals, and this is probably right. Theoretically it should make no difference, for the viral infections have long incubation periods and are generally most contagious just before the major symptoms and signs appear, as Doctor Scott has implied. However, the possibility of spread from patient to medical personnel to other patients cannot be excluded, and at a minimum these severely ill patients should be in a single room, even when strict isolation techniques are impractical.

Doctor Wolf has asked if there is a relationship between influenza virus infections and *Hemophilus influenzae*. The evidence is certainly not clear, but during the influenza pandemic of 1918 many investigators felt that *H. influenzae* was isolated more frequently from cultures than would be expected. Subsequent studies in later, milder epidemics suggest a similar relationship. What this means, we don't know. Certainly no pathogenic activity can be ascribed to *H. influenzae*, for patients with influenza virus infections do not die with H. influenzae infections. This potential synergistic microbial relationship, like the problem of laboratory diagnosis of influenza, remains to be solved as we develop newer techniques and more sensitive tests.

Dr. Wolf: We would like to continue this interesting discussion but time is up. I want to thank those who have presented and discussed cases. We have learned that these epidemic diseases are presumably due to viruses but no during early fall to the influenza group of viruses. They are thought to be spread by droplet infection, but one wonders in view of their similarity to dengue whether or not some of them may be spread by mosquitoes or other insect vectors. As far as treatment is concerned it is clear from some of Doctor Haight's earlier studies and those of others that antibiotics have no curative value whatever. Neither is there evidence that antibiotics reduce the incidence of the relatively rarely occurring bacterial complications. Nevertheless antibiotics will probably continue to be widely used — just in case.

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*Swartout, R., III, and Gunther, K.: "Dizziness:" Vertigo and Syncope, GP *8*:35 (Nov.) 1953.

Association Activities

PRESIDENT'S LETTER

The midwinter meeting of the House of Delegates was held in Oklahoma City on December 12. It is always gratifying to the officers of the Association and to the Executive Office that so many busy doctors are willing to donate their time to conducting the affairs of the Association. If you will remember, the twelfth of December was very cold, and the roads were either icy or snowy, but it did not deter 75 doctors from all parts of the state from appearing at the meeting.

The House of Delegates enthusiastically accepted the recommendation of the Building Committee that a building site be purchased and plans be obtained for our new office.

Our only out of state speaker was Mr. John Parrish, secretary of the St. Paul Mercury Indemnity Company. Mr. Parrish was very complimentary in telling us that the company was satisfied with its loss ratio in Oklahoma, and that this could not be said about other areas in the nation. He felt that it was due to the cooperation among our doctors, and the result of the doctors' understanding of the basic problems concerning malpractice suits. Our Executive Office plans to reprint Mr. Parrish's paper, and I urge you to read it carefully.

Many other things were discussed and will be reported to you at the County Society meetings by delegates and members of the Council.

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Book Reviews

PRACTICE OF ALLERGY. Warren T. Vaughan, M.D., Revised by J. Harvey Black, M.D. Third Editon. 1954. C. V. Mosby Company, St. Louis, Missouri. Price $21.00.

Doctor Vaughan in 1930 wrote *Allergy And Applied Immunology.* At that time, little was known of allergy and the book was written to be used both by the physician and the patient. As an outgrowth of *Allergy And Applied Immunology,* Doctor Vaughan wrote *Practice of Allergy* for the benefit of the medical profession. Its companion and smaller volume, *Primer of Allergy,* was written primarily for the patient.

Practice of Allergy was originally written in 1939 and has been revised and brought up to date by Dr. J. Harvey Black. It is a "must" for any physician who is practicing allergy. The book covers all of the ramifications of allergic disease and has the most complete bibliography of any volume of a similar nature. Its use is not limited to those specializing in allergy as it contains a wealth of information which should be helpful to all physicians, regardless of their type of practice.

The revised chapter on Fungus Allergy is helpful in view of the more recent emphasis being placed on this subject. The chapter on Pulmonary Function Studies is a valuable addition.

The greatest objection is its price; however, I feel that its value as an excellent reference text as well as the most complete volume pertaining to the various allergic diseases, far outweighs this objection.

—Vernon D. Cushing, M.D.

PRIMER OF ALLERGY. Warren T. Vaughan, M.S., MD., Revised by J. Harvey Black, M.D. Fourth Edition, 1954. C. V. Mosby Company, St. Louis, Missouri. Price $4.25.

This small volume of 191 pages was written primarily for the allergic patient. As Doctor Vaughan stated in his preface to the first edition, this book is an outgrowth of his original text, *Allergy and Applied Immunology.*

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The author has attempted to explain in simple language what happens in allergic disease and in the allergic individual. The book is adequately illustrated, including some cartoons pertaining to allergic situations by the late H. T. Webster. Many of the chapters are concluded with a question and answer section which patients should find helpful.

Doctor Black has done an excellent job in revising this book, bringing into the fourth edition the newer aspects of drug treatment and changes more in keeping with the present concepts of allergic disease.

I believe that the book is of definite value and can be recommended without reservation to the allergic patient.

—Vernon D. Cushing, M.D.